

**REMARKS**

The Office Action mailed February 19, 2008 has been carefully considered and the following response prepared.

**Objections to specification – 37 CFR 1.821-1.825**

At page 2 of the Office Action, the Examiner objected to the specification as failing to comply with 37 CFR 1.821-1.825 because the specification contains nucleotide and amino acid sequences that do not include sequence identifiers.

The specification has been amended to insert sequence identifiers. Withdrawal of this objection to the specification is respectfully requested.

**Claim objections**

At page 2 of the Office Action, the Examiner objected to claims 5, 11 and 14 because of informalities. Claims 5 and 11 have been amended, as requested by the Examiner to delete “SEQ ID No. 1” and “SEQ ID No.2” and insert --SEQ ID NO: 1-- and “SEQ ID NO: 2--. Claim 14, part (b) has been amended to insert --and-- at the end of the line. Withdrawal of the objections to the claims is respectfully requested.

**Rejection under 35 USC 102(e)**

At page 3 of the Office Action, the Examiner rejected claims 1-3, 6-8 and 13-15 under 35 USC 102(e) as anticipated by Daniell (U.S. Patent 7,129,391) (the ‘391 patent”) filed May 15, 1998). The Examiner asserted that the ‘391 patent claims soybean, peanut and pea plants whose chloroplasts are stably transformed (claims 75-77 and 81-83) and a method of producing them (claim 92). The Examiner alleged that the ‘391 patent indicates that stably transformed plants have progeny with the transformation event (column 7, line 10-13); thus, the plants must be

fertile. The Examiner further asserts that the '391 patent also claims plastid transformation vectors comprising an expression cassette encoding a selection marker, and two sequences homologous with a portion of a legume plastome, wherein the sequences flank an expression cassette encoding a peptide of interest.

Applicants traverse this rejection. Claims 1-3 and 6 are directed to fertile transplastomic leguminous plants. Claims 7, 8 and 13 are directed to transformation vectors suitable for leguminous plant plastid transformation that comprise at least two sequences homologous with a zone of the plastome of the leguminous plant to be transformed bordering at least one expression cassette. Claims 14 and 15 are directed to methods for obtaining fertile transplastomic leguminous plants.

Applicants respectfully submit that the '391 patent does not anticipate claims 1-3, 6-8 and 13-15 because it does not contain an enabling disclosure of fertile transplastomic leguminous plants. In order to anticipate a claimed invention a cited reference must contain an enabling disclosure of the claimed invention. See MPEP 2121. Additionally, the '391 patent does not disclose the vectors and methods of claims 7-8 and 13-15.

The '391 patent discloses universal chloroplast integration and expression vectors which are stated to be competent to stably transform and integrate genes of interest into chloroplast genomes of multiple species of plants. The universal vector comprises an expression cassette flanked on each side by a flanking sequence. The flanking sequences are selected from transcriptionally active regions of a chloroplast that is highly conserved in a broad range of chloroplast genomes of higher plants. A preferred region is the spacer 2 region, the intergenic spacer region between the t-RNA<sup>Ile</sup> and tRNA<sup>Ala</sup> region. The only exemplified universal chloroplast vectors in the '391 patent contains flanking sequences from the tobacco chloroplast genome.

Example 6 of the '391 patent, the only example related to soybean, briefly describes general steps of a plastidial transformation of soybean leaves with a universal chloroplast transformation that contains tobacco chloroplast flanking sequences. Figure 15 shows that some

soybean embryonic shoots are resistant to the antibiotic used for selection. There is no disclosure of developed and fertile soybean plants. Similarly, Example 5 of the Daniell '391 patent, directed to peanut chloroplast transformation, also only briefly describes general steps of a plastidial transformation with the same universal chloroplast transformation vector. Figure 14 shows that some peanut embryonic shoots are resistant to the antibiotic used for selection. There is no disclosure of developed and fertile peanut plants. Despite the language at column 7, lines 10-13, Daniell did not obtain fertile transplastomic leguminous plants. As discussed below, fertile transplastomic legume plants were first obtained several years after the filing date of the '391 patent. Consequently, the '391 patent does not enable fertile transplastomic leguminous plants.

Zhang et al. (J. Plant Biotechnology 3(1), 39-44, (2001), a copy of which was previously submitted in an Information Disclosure Statement, reported an attempt to transform plastids of soybean suspension cultures. Zhang et al. did not obtain fertile transplastomic soybean plants. The publication also reports on page 42 (right column, second paragraph), that plastid transformation was reported in 2001 on only four species, namely tobacco, rice, *Arabidopsis*, and potato, and that only tobacco had been reported to generate fertile plants.

Henry Daniell, the inventor of the '391 patent, published a scientific review article with Nathalie Dufourmantel, one of the inventors of the present application, about the agronomically important crops in which plastids have been successfully transformed. A copy of this publication, Daniell et al., TRENDS in Biotechnology, 23(5): 238-245, (2005), is submitted in the accompanying Information Disclosure Statement. This publication specifically reports on page 242 that a first attempt to transform plastids of soybean cells was made by Zhang et al., but that the first successful generation of fertile chloroplast transgenic plants of soybean was reported by Dufourmantel et al., Plant Mol. Biol. 55: 479-489, (2004). Hence, the inventor Daniell implicitly acknowledged in his 2005 publication that his prior '391 patent was not a disclosure of fertile transplastomic soybeans, and that the first such disclosure was the work of Dufourmantel et al.

Dufourmantel et al. *Plant Mol. Biol.* 55: 479-489, (2004), published by several of the inventors, discloses work which forms the basis of the present application. (The article was published after the filing date of PCT/EP 03/15007, of which the present application is the national phase in the United States.) A copy of Dufourmantel et al. is submitted in the accompanying Information Disclosure Statement. At page 480, left column, second paragraph, the publication lists the species which have been shown in the scientific community to have been made both transplastomic and fertile. Apart from tobacco, *Lycopersicon esculentum* and *Lesquerella fendleri* were the only other transplastomic plants shown to be fertile and capable of transgene transmission to the next generation. Soybean was clearly not among those species made both transplastomic and fertile before the publication of the article.

The '391 patent does not anticipate the vectors of claims 7-8 and 13. The universal chloroplast vector disclosed in the '391 patent contains tobacco chloroplast flanking sequences, whereas the vectors of claims 7-8 and 13 contain sequences homologous with a zone of the plastome of the leguminous plant to be transformed.

The '391 patent also does not anticipate the methods of claim 14 and 15, as the methods in the '391 patent did not result in fertile transplastomic leguminous plants, and the methods were not performed with embryogenic tissues obtained from immature embryos of leguminous plants as required by claims 14-15.

In view of the above, the '391 patent does not qualify as an anticipatory reference against the claims of the present application because it does not enable fertile transplastomic leguminous plants. In order to anticipate a claimed invention a cited reference must contain an enabling disclosure of the claimed invention. The scientific literature substantiates the lack of an enabling disclosure of fertile transplastomic leguminous plants in the '391 patent. Additionally, the '391 patent does not disclose the claimed vectors or methods.

Claims 1-3, 6-8 and 13-15 are not anticipated by the Daniell '391 patent. Withdrawal of this section 102(e) rejection is respectfully requested.

**Rejection under 35 USC 103**

At pages 3-5 of the Office Action, the Examiner rejected claims 1-16 under 35 USC 103 as obvious over Maliga et al. (U.S. Patent 5,877,402; the '402 patent) in view of von Allmen (GenBank Accession No. X7675). The Examiner alleged that it would have been obvious to one of ordinary skill in the art to modify the method of plastid transformation taught by Maliga et al, to replace the tobacco flanking regions with the corresponding ones from soybean plastid as described in von Allmen. The Examiner alleged that persons skilled in the art would be motivated to do so because plastid transformation works by homologous recombination and one skilled in the art would understand that the targeting sequences should have high homology with the target and would use soybean targeting sequences with soybean, the sequences taught by von Allmen.

Applicants traverse this rejection. Claims 1-16 are directed to fertile transplastomic leguminous plants, transformation vector suitable for leguminous plant plastid transformation, and methods for obtaining fertile transplastomic leguminous plants.

Maliga et al., U.S. Patent 5,877,402, discloses DNA constructs for transformation of plastids of multicellular plants and expression of foreign proteins in plastids. The DNA constructs comprise a transforming DNA which is targeted to a pre-determined location on the plastid genome and inserted into the plastid genome by homologous recombination with targeting segments comprising DNA sequences homologous to the predetermined region of the plastid genome. The transforming DNA contains a non-lethal selectable marker gene which confers a selectable phenotype on cells having plastids in which substantially all of the genomes therein contain the transforming DNA and at least one insertion site for an additional DNA segment such as a DNA encoding a heterologous protein. Maliga et al. discloses plastid transformation in tobacco using DNA constructs in which the targeting sequences were tobacco plastid genome sequences.

von Allmen, GenBank Accession No. X7675, discloses soybean plastid DNA for rps12, rps7, 16s rRNA, tRNA-Val, NADH dehydrogenase and ORF 143.

Claims 1-16 are not obvious in view of Maliga et al., the '402 patent, and von Allmen. Persons skilled the art would not be led to combine the teachings of Maliga et al. with the soybean plastid DNA of von Allmen, because, at the time the present application was filed, there was no reasonable expectation that fertile transplastomic leguminous plants could be obtained. As discussed above, prior to the present application, persons skilled in the art had tried but failed to produce fertile transplastomic leguminous plants. The '402 patent, which was filed in 1994, well before the present application, thus does not enable the claimed fertile transplastomic leguminous plants for the same reasons discussed above in relation to the '391 patent. Persons skilled in the art would have no reason to combine the disclosures of the '402 patent and von Allmen. Persons skilled in the art would also not be led to combine the teachings of the '402 patent and von Allmen to produce the methods and vectors of claims 7-16, since there was no reasonable expectation of successfully producing fertile transplastomic leguminous plants.

Applicants were the first to obtain fertile transplastomic leguminous plants. Prior to the present application, there were no reports of fertile transplastomic leguminous plants, despite attempts by Zhang et al. and attempts by Daniell in the '391 patent, which Daniell implicitly admitted were non-enabling in his latter publication Daniell et al., discussed above. In view of the failure of others skilled in the art, there would be no reasonable expectation that such plants could be obtained. It would therefore not be obvious for persons skilled in the art to combine the teachings of the '402 patent and von Allmen to produce the claimed fertile transplastomic leguminous plants, vectors and methods.

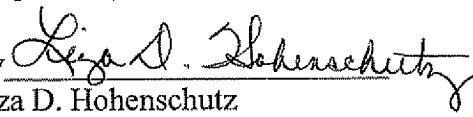
Claims 1-16 are not obvious in view of the '402 patent and von Allmen. Withdrawal of this section 103 rejection is respectfully requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 03-2775, under Order No. 05500-00148-US. A duplicate copy of this paper is enclosed.

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Respectfully submitted,

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